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(54) Title: NEW USE OF 4, 5, 6, 7-TETRAHYDROIMIDAZO-[4,5-C]PYRIDINE DERIVATIVES

(57) Abstract: The invention relates to the use of compounds of Formula (I), in which R^1, R^2, R^3 and R^4 are as described in the specification, for the treatment or prophylaxis of SSAO-mediated complications, such as diabetes.

NEW USE

TECHNICAL FIELD

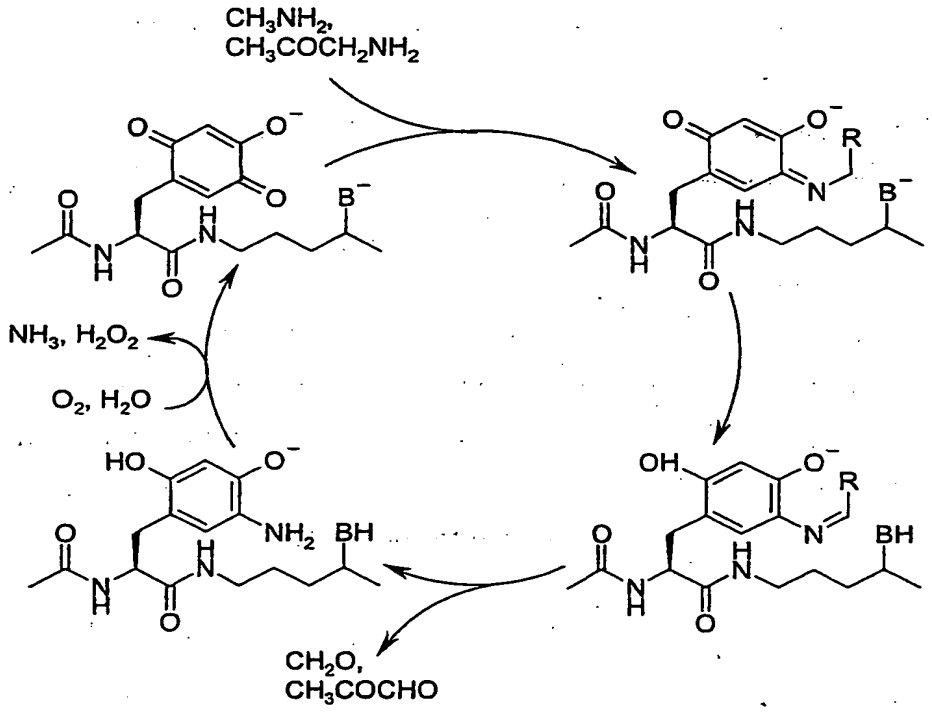
The present invention relates to use of 4-alkyl-5-alkoxycarbonyl-4, 5, 6, 7-tetrahydroimidazo[4,5-c] pyridine derivatives for the manufacture of medicaments for, or treatment or prophylaxis of semicarbazide-sensitive amine oxidase (SSAO)-mediated complications.

BACKGROUND ART

Semicarbazide-sensitive amine oxidase, SSAO, is a monoamine oxidase that recently has been suggested to be responsible for microvascular complications in diabetic patients. Nephropathy, neuropathy and retinopathy represent the end results of microvascular complications in both insulin dependent diabetes mellitus (IDDM) and non-insulin dependent diabetes mellitus (NIDDM). Heart attack, angina, strokes, amputations, blindness and renal failure are clinical events that represent the end point of the clinical study. Endothelial cells dysfunction may precede the diabetic state of complications. The SSAO enzyme is located in the vascular smooth muscles, retina, kidney and the cartilage tissues, and in the circulating blood (Yu, P. H. Deamination of methylamine and angiopathy; toxicity of formaldehyde, oxidative stress and relevance to protein glycoxidation in diabetes. *J. Neural. Transm. Suppl.*, **1998**, *52*, 201) and has been found to be overactive in diabetic patients (Ekblom, J. Potential therapeutic value of drugs inhibiting semicarbazide-sensitive amine oxidase: vascular cytoprotection in diabetes mellitus. *Pharmacol. Res.*, **1998**, *37*, 87). SSAO oxidizes a primary amine into the corresponding aldehyde with the help of the non-proteogenic amino acid topaquinone (*Scheme 1*). Oxidation of the aminophenol form of topaquinone into the quinone form, in order to close the catalytic cycle, is catalyzed by Cu(II), present in the active site of the enzyme. Hydrogen peroxide and ammonia are produced. The general catalytic cycle is very similar to the one observed for other monoamine oxidases *(Scheme 1)*. The higher activity of SSAO as well as the higher concentration of its natural substrates, methylamine and aminoacetone, in diabetic patients, would lead to a higher production of formaldehyde, methylglyoxal and hydrogen peroxide. These products are known to be highly cytotoxic for the endothelial cell layer and might lead to the observed microvascular complication in diabetic patients (Yu, P. H. Deamination of methylamine and angiopathy; toxicity of formaldehyde, oxidative stress and

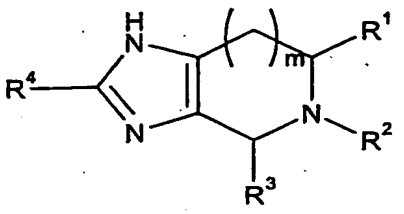
relevance to protein glycoxidation in diabetes. *J. Neural. Transm. Suppl.*, **1998**, *52*, 201). The inhibition of SSAO-mediated reactions is therefore a strategy that could be beneficial for a variety of pathological conditions.

Scheme 1: SSAO's catalytic cycle. The active site is represented schematically by the topaquinone residue as well as by a basic amino acid residue B^- essential for the activity.



SUMMARY OF THE INVENTION

According to the invention a method of treatment or prophylaxis of SSAO-mediated complications in mammals including humans is provided. The method comprises administering to a patient in need of such treatment a therapeutically effective amount of a compound of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is

(a) H, or

(b) CONH–R^5;

R^2 is

(a) $COOR^5$,

(b) COR^5,

(c) CONH–R^5,

(d) CSNH–R^5, or

(e) H;

R^3 is

(a) H,

(b) C_{1-8} alkyl, or

(c) $(CH_2)_nAr$;

R^4 is

(a) H,

(b) Ar, or

(c) C_{1-8} alkyl; and

R^5 is

(a) H,

(b) $(CH_2)_nAr$,

(c) $(CH_2)_nOAr$,

(d) C_{1-8} alkyl containing 0-2 oxygen atoms and optionally substituted with 0-5 halogen atoms, or

(e) a polyether chain having the formula $(CH_2)_xO(CH_2)_yO(CH_2)_zCH_3$;

n is an integer 0 to 4;

m is an integer 0 to 2;

x and y are integers 2 to 4;

z is an integer 0 to 3;

Ar is phenyl, 1-naphthyl or 2-naphthyl, unsubstituted optionally mono-or poly-substituted with electrodonating groups, halogen, C_{1-6} alkyl, CF_3, hydroxyl, C_{1-6} alkoxyl, OCF_3, CN, NO_2, phenyloxyl, benzyloxyl, optionally substituted phenyl, alkylsulfonyl, C_{1-6} alkenyl, -NH_2, R^7NH-, R^7 R^7N-, C_{1-6} alkylcarboxyl, formyl, C_{1-6}

alkyl-CO-NH-, aminocarbonyl (R^7 R^7-N-CO-), SR^7 wherein R^7 is simultaneously or alternatively H or C_{1-6} alkyl; cynnamoyl, unsubstituted or optionally substituted benzyl; 1,1-diphenylethyl, a monocyclic or bicyclic heterocyclic ring (furyl, pyrrolyl, triazolyl, diazolyl, oxazolyl, thiazolyl, oxadiazolyl, isothiazolyl, isoxazolyl, thiadiazolyl, pyridyl, pyrimidyl, pyrazinyl, thienyl, imidazolyl, pyrazolyl, indolyl, quinolinyl, isoquinolinyl, benzofuryl, benzothienyl, benzoxadiazolyl which are unsubstituted or optionally mono or di-substituted with halogen, C_{1-6} alkyl); 2, or 3, or 4-pyridyl or a 5 to 7-membered unsaturated or partially or completely saturated heterocyclic ring each containing 1 to 4 heteroatoms selected from oxygen, nitrogen or sulfur where nitrogen containing heterocycles may contain H or C_{1-6} alkyl or CF_3-CO- at the nitrogen atoms where such a substitution is allowed.

The term "C_{1-8} alkyl" denotes a saturated or unsaturated, straight, branched or cyclic alkyl group having from 1 to 8 carbon atoms. Examples of said C_{1-8} alkyl include methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, t-butyl, and straight- and branched-chain pentyl, hexyl, septyl and octyl, optionally substituted with 0-5 halogen atoms.

The term "halogen" shall mean fluorine, chlorine, or bromine.

DETAILED DESCRIPTION OF THE INVENTION

According to the present invention it has been found that 4-alkyl-5-alkoxycarbonyl-4,5,6,7-tetrahydroimidazo[4,5-c] pyridine derivatives of Formula (I) are potent compounds for inhibiting SSAO-mediated reactions.

4-alkyl-5-alkoxycarbonyl-4,5,6,7-tetrahydroimidazo[4,5-c] pyridine derivatives are known from GB 2 158 440 and U.S. 4,223,146. In the GB application the compounds are disclosed to have anti-viral activity. The compounds in the U.S. patent are useful as antiulcer agents and as inhibitors of gastric secretion.

In Formula (I) preferred substituents are as follows:

R^1 is H, CO-NH2, R^3 is C_{1-3} alkyl or benzyl and R^2 is $COOR^5$ and R^5 is

1) H or a linear, branched or cyclic C_{1-8} alkyl which can be saturated or not, containing 0-2 oxygen atoms and optionally substituted with 0-5 halogen atoms;

2) (CH_2)nAr, where n = 0-3 and Ar is a phenyl group or a phenyl group substituted with electrodonating groups and/or halogen atoms.

Preferred compound of Formula (I) are:

benzyl 4-methyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate;

benzyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate;

benzyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate;

2,2,2-trichloroethyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate; and

benzyl (4S,6S)-6-(aminocarbonyl)-4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate.

The compounds of the Formula (I) can form acid addition salts with acids such as conventional pharmaceutically acceptable acids, for example maleic, hydrochloric, hydrobromic, phosphoric, acetic, fumaric, salicylic, citric, lactic, mandelic, tartaric and methanesulfonic.

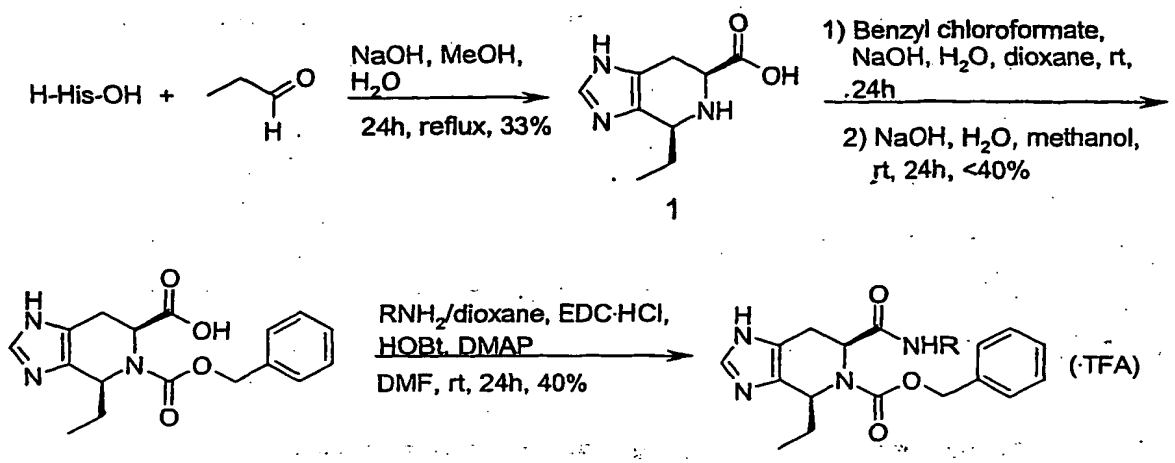
Compounds of Formula (I) may also form solvates such as hydrates and the invention also extends to these forms. When referred to herein, it is understood that the term "compound of Formula (I)" also includes these forms.

Certain compounds of Formula (I) are capable of existing in stereoisomeric forms including diastereomers and enantiomers and the invention extends to each of these stereoisomeric forms and to mixtures thereof including racemates. The different stereoisomeric forms may be separated one from the other by the usual methods. Any given isomer may be obtained by stereospecific or asymmetric synthesis. The invention also extends to any tautomeric forms and mixtures thereof.

Preferably the compounds of Formula (I) are used for treatment or prophylaxis of SSAO mediated vascular complications and for insulin dependent diabetes mellitus and non-insulin dependent diabetes mellitus.

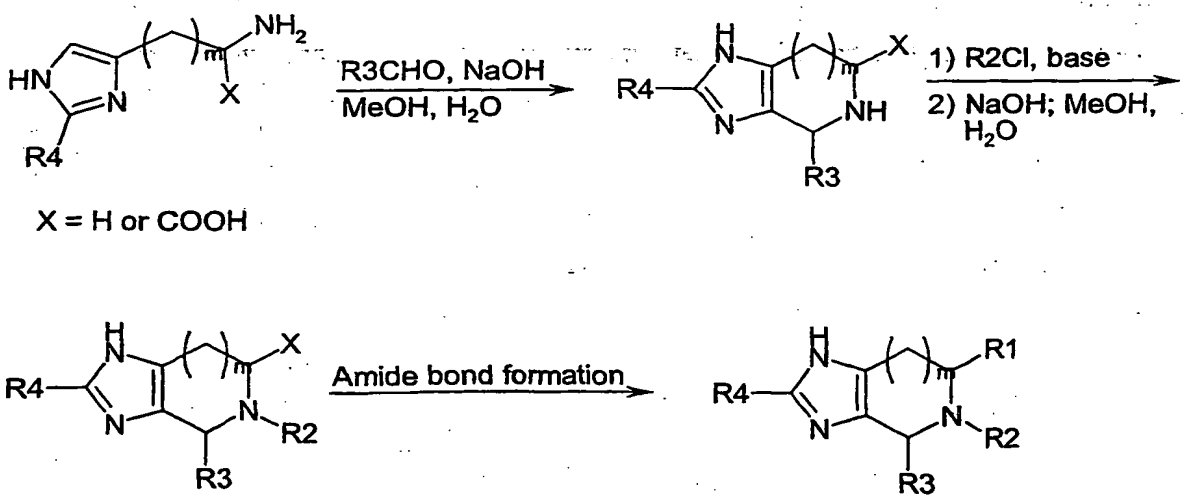
The compounds used in the invention are prepared according to known methods. The compounds can be prepared as follows:

Scheme 2:



R = iBu: Benzyl (4S,6S)-4-ethyl-6-[(isobutylamino)-carbonyl]-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate
R = H: Benzyl (4S,6S)-6-(aminocarbonyl)-4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate

Scheme 3:



The starting materials are commercially available or can be prepared following known procedures.

According to the present invention the compounds for treatment of SSAO mediated complications can conveniently be administered in a pharmaceutical composition containing the compound in combination with a suitable excipient. Such pharmaceutical compositions can be prepared by methods and contain excipients which are well known in the art. A generally recognized compendium of such methods and

ingredients is Remington's Pharmaceutical Sciences by E.W. Martin (Mark Publ. Co., 15th Ed., 1975). The compounds and compositions can be administered orally, parenterally (for example, by intravenous, intraperitoneal or intramuscular injection), topically, or rectally.

Useful dosages of the compounds of Formula (I) can be determined by comparing their *in vitro* activity, and *in vivo* activity in animal models. Methods for the extrapolation of effective dosages in mice, and other animals, to humans are known in the art; for example, see U.S. Pat. No. 4,938,949.

The compound can be administered in unit dosage form; for example, containing about 0.05 mg to about 500 mg, conveniently about 0.1 mg to about 250 mg, most conveniently, about 1 mg to about 150 mg of active ingredient per unit dosage form. The desired dose may be presented in a single dose or as divided doses administered at appropriate intervals. The compositions can be administered orally, sublingually, transdermally, or parenterally at dose levels of about 0.01 to about 150 mg/kg, preferably about 0.1 to about 50 mg/kg, and more preferably about 0.1 to about 30 mg/kg of mammal body weight.

The invention will now be illustrated with the following examples, which however, are not intended to limit the scope of the invention.

The following abbreviations are used:

aq: aqueous; br: broad; DIPEA: diisopropylethylamine; DMAP: 4-(*N,N*-dimethylamino)pyridine; ECAO: *Esterichia Coli* amine oxidase; EDC·HCl: *N*-ethyl-*N'*-3(dimethylamino)propylcarbodiimide hydrochloride; EI: electron impact; eq: equivalent; EtOAc: ethyl acetate; HOBt: hydroxybenzotriazol; HTS: high throughput screening;; Mp: melting point; HRMS: high resolution mass spectrum; org: organic; RP-HPLC: reversed-phase high pressure liquid chromatography; SAR: structure activity relationship; sat: saturated; TLC: thin layer chromatography.

Experimental: Solvents were purchased from *Merck* or *Riedel-de Haen*. Chemicals and reagents were purchased from *Aldrich*, *Lancaster* or *Fluka*. The buffer solution (pH 9) was bought from *Merck* (catalogue number 1.09461.1000, boric acid/KCl/NaOH). TLCs were run using Silicagel60 F_{254} plates purchased from *Merck*. TLCs were analyzed by UV or stained with a solution of $KMnO_4$ in water. Flash chromatography was run using Silicagel 60 (230-400 mesh) from *Merck*. Parallel flash chromatography was run on a Foxy-200 system from *Isco Inc.* with 108-disposable

columns for FC from *Isco Inc.* RP-HPLCs were run on a *Gilson* system, using a 119 UV-detector (214 nm or 254 nm), a 805 manometric module, a 305- and a 306-pumps and a *Vydac* C_{18}-column (218TP1022); H_2O+0.1%TFA/CH_3CN were used as eluents. Mps were measured with a *Gallenkamp* apparatus and were uncorrected. NMR spectra were recorded on a *Varian* Inova 400 instrument. EI-MS spectra were recorded on a JMS SX-102A mass spectrometer (*Jeol*, Tokyo, Jpn) at 70eV or on an Autospec-oaTOF *Micromass Manchester instrument* at 70 eV. HRMS spectra were recorded on a LCT *Micromass instrument* with flow injection-electrospray positive mode; quaternary ammonium salts were used as references. Reactions were followed by MS, using a Platform I *Micromass instrument*, Manchester, with an electrospray positive and negative mode flow injection. Elemental analysis was run on an *Elementar* Vario EL instrument.

General Procedure I (GPI): A solution of histidine or histamine, NaOH and aldehyde was prepared in water and MeOH, and was heated under reflux for 24 h. After cooling the solution to room temperature, then to 0°C, aq. conc. HCl was added. See the specific examples for the work-up procedures.

General procedure II (GPII): A solution of tetrahydroimidazopyridine and K_2CO_3 in $CHCl_3$ and water was cooled to 0°C. The chloroformate, resp. the acyl chloride was added dropwise. The mixture was stirred for 24 h while warming up to room temperature. The phases were separated, the org. phase dried over Na_2SO_4 and the solvent removed under reduced pressure. The residue was dissolved or suspended in MeOH (3 mL/mmol of starting material) and aq. 1M NaOH (2 mL/mmol of starting material) was added. After 1 h, the mixture was worked-up and purified, see specific examples.

Carboxylic acid Intermadiate (scheme 2)

(*4S,6S*)-4-Ethyl-4,5,6,7-tetrahydro-3H-imidazo[4,5-c]pyridine-6-carboxylic acid: According to *GPI* with histidine (15.5 g, 0.100 mol), NaOH (24 g, 0.60 mol), water (100 mL), MeOH (400 mL) and propionaldehyde (20 mL, 0.276 mol). The solution was then acidified to pH 7-8 with aq. conc. HCl (60 mL) and the solvent was removed under reduced pressure. After drying the residue thoroughly under high vacuum, the oil was triturated with hot EtOH and filtered (3x). The filtrate was evaporated under reduced pressure and the residue crystallised from EtOH/water. **(*4S,6S*)-4-Ethyl-4,5,6,7-tetrahydro-3H-imidazo[4,5-c]pyridine-6-carboxylic acid** was isolated as a white

powder (6.44 g, 33%). ^{1}H-NMR and NOE-measurement showed a *cis/trans* ratio of 9:1. Mp = 242-4 °C. ^{1}H-NMR (400 MHz, D_2O; only *cis*-stereoisomer described): δ = 7.75 (s, 1H); 4.43 (m, br., 1H); 4.05 (dd, J_1 = 12.1 Hz, J_2 = 5.2Hz, 1 H); 3.81 (dd, J_1 = 16.5 Hz, J_2 = 5.3 Hz, 1H); 3.00 (ddd, J_1 = 16.5 Hz, J_2 = 12.1 Hz, J_3 = 2.4 Hz, 1H); 2.27 (m, 1H); 1.91 (m, 1H); 1.14 (t, J = 7.6 Hz, 3H). ^{13}C-NMR (100 MHz, D_2O): δ = 173.28 (s); 137.27 (d); 129.83 (s); 124.10 (s); 57.98 (d); 56.20 (d); 25.17 (t); 23.79 (t); 9.51 (q). MS (EI): m/z = 194 (M^+-H_2, 2%); 166 (61%); 148 (9%); 120 (100%); 107 (10%); 93 (10%). HRMS: Calc. for $C_9H_{13}N_3O_2$: M^+ = 195.1008; found: M^+ = 195.0000.

Intermediate 2 (Scheme 2)

(*4S,6S*)-5-[(Benzyloxy)carbonyl]-4-ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-6-carboxylic acid: A solution of **(*4S,6S*)-4-Ethyl-4,5,6,7-tetrahydro-3H-imidazo[4,5-c]pyridine-6-carboxylic acid** (500 mg, 2.56 mmol) in an aq. buffer solution at pH9 (5 mL) and dioxane (1 mL) was cooled to 0 °C. Benzyl chloroformate (0.845 mL, 5.64 mmol) was added dropwise over 1 min. The pH was maintained between 7 and 9 by adding from time to time aq. 1M NaOH (total amount: about 5 mL). The mixture was stirred overnight while the temperature rose slowly to room temperature. The final pH was equal to 6.5 and an oily precipitate was lying in the bottom of the flask. This oily precipitate was decanted, dissolved in $CHCl_3$ and the solution dried over $MgSO_4$. After filtration, the filtrate was evaporated under reduced pressure. The residue was diluted in MeOH (20 mL) and aq. 1M NaOH was added (10 mL). This solution was stirred at room temperature overnight and the pH was brought to 7 with aq. 1M HCl. The solvent was removed under reduced pressure and the residue dried under high vacuum. The dried residue was purified by RP-HPLC (C_{18}-column, 95% H_2O → 75% H_2O over 10 min → 0% H_2O over 10min). The acid was obtained as a foam (224 mg, 40%). ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.15 (s, br., 1H); 7.40-7.23 (m, 5H); 5.46 (s, br., 1H); 5.21 (s, br., 3H); 2.83 (dd, J_1 = 15.6 Hz, J_2 = 6.1 Hz, 1H); 1.79 (s, br., 2H); 1.05 (s, br., 3H). MS (pos. ionization): m/z = 330 (MH^+).

Example 1:

4-Methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride: According to *GPI* with histamine dihydrochloride (12.1 g, 0.109 mol), NaOH (10.9 g, 0.272 mol), water (100 mL), MeOH (450 mL) and acetaldehyde (15.5 mL, 0.276 mol). The solution was acidified to pH<1 with aq. conc. HCl and the solvent was removed under reduced pressure. The residue was thoroughly dried under high vacuum. The

resulting oil was triturated with MeOH (1x 150 mL, 2x 50 mL) and filtered. The filtrate was evaporated under reduced pressure and the residue dried under high vacuum. This residue was then suspended in ^{i}PrOH and this suspension refluxed for 1h. After allowing it to cool to room temperature, the mixture was filtered and the precipitate dried under high vacuum. The product was obtained as a brown powder that was not purified further (21.2 g, 90%). ^{1}H-NMR (400 MHz, D_2O): δ = 8.70 (s, br., 1H); 3.76 (m, br., 1H); 3.53 (m, br., 1H); 3.09 (s, br., 2H); 1.69 (s, br., 3H).

Example 2:

4-Ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride: According to *GPI* with histamine dihydrochloride (20.0 g, 0.109 mol), NaOH (19.6 g, 0.49 mol), water (100 mL), MeOH (450 mL) and propionaldehyde (20.0 mL, 0.276 mol). The reaction mixture was acidified to pH<1 with aq. conc. HCl (200 mL) and the solvent was removed under reduced pressure. The residue was dried thoroughly under high vacuum and the resulting oil triturated with MeOH (1x150 mL and 2x50 mL). The filtrate was evaporated under reduced pressure and the residue dried under high vacuum. The resulting oil was triturated with EtOH (1x50 mL and 2x15 mL) and filtered. The precipitate was dried under high vacuum. **4-Ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** was obtained as a colorless powder (5.38 g, 22%). ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.95 (s, 1H); 4.69-4.61 (m, 1H); 3.80-3.70 (m, 1H); 3.55-3.46 (m, 1H); 3.20-3.02 (m, 2H); 2.31-2.15 (m, 1H); 2.05-1.92 (m, 1H); 1.15 (t, J = 7.8 Hz, 3H). ^{13}C-NMR (100 MHz, D_2O): δ = 134.70 (d); 124.98 (s); 123.72 (s); 53.26 (d); 40.59 (t); 24.41 (t); 18.11 (t); 8.88 (q). MS (EI): m/z = 151 (M^+, 1%); 150 (2%); 122 (100%); 107 (5%); 95 (13%); 80 (3%). HRMS: calc. for $C_8H_{13}N_3$: M^+ = 151.1158; found: 151.1109.

Example 3:

4-Propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride: According to *GPI* with histamine dihydrochloride (20.0 g, 0.109 mol), NaOH (19.6 g, 0.49 mol), water (100 mL), MeOH (450 mL) and butyraldehyde (24.9 mL, 0.278 mol). The reaction mixture was acidified to pH<1 with aq. conc. HCl (200 mL) and the solvent was removed under reduced pressure. The residue was dried thoroughly under high vacuum and the resulting oil triturated with MeOH (1x150 mL and 2x50 mL). The filtrate was evaporated under reduced pressure and the residue dried under high vacuum. The resulting oil was triturated with EtOH (1x50 mL and 2x15 mL) and

filtered. The precipitate was dried under high vacuum. **4-Propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** was obtained as a colorless powder (20.9g, 80%). ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.99 (s, 1H); 4.75 (dd, J_1 = 9.0 Hz, J_2 = 4.4 Hz, 1H); 3.82-3.73 (m, 1H); 3.59-3.50 (m, 1H); 3.24-3.05 (m, 2H); 2.21-2.10 (m, 1H); 2.04-1.90 (m, 1H); 1.70-1.52 (m, 2H); 1.07 (t, J = 7.8 Hz, 3H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 136.13 (d); 126.43 (s); 125.61 (s); 53.05 (d); 41.79 (t); 34.41 (t); 19.45 (t); 19.30 (t); 14.01 (q). MS (EI): m/z = 165 (M^+, 1%); 164 (2%); 135 (2%); 122 (100%); 95 (12%); 80 (2%); 68 (5%).

Example 4:

4-Phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride: According to *GPI* with histamine (10.0 g, 90 mmol), NaOH (9.0 g, 225 mol), water (90 mL), MeOH (365 mL) and benzaldehyde (23.1 mL, 0.23 mol). The reaction mixture was acidified to pH<1 with aq. conc. HCl (165 mL) and the solvent was removed under reduced pressure. The residue was dried thoroughly under high vacuum and the resulting oil triturated with hot ^{i}PrOH (150 mL). The mixture was filtered and the precipitate washed with cold ^{i}PrOH (2x30 mL). The filtrate was heated to reflux and hexane (210 mL) added slowly, whereas a precipitate formed. The mixture was cooled to room temperature, then to −18 °C. The precipitate was filtered and dried. **4-Phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** was obtained as a yellow powder that contained 0.7 eq of ^{i}PrOH (14.1 g, 12.2 g of product, 50%). ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.96 (s, 1H); 7.6-7.3 (m, 5H); 5.99 (s, 1H); 3.75-3.60 (m, 2H); 3.38-3.30 (m, 1H); 3.20 (dt, J_1 = 16.6 Hz, J_2 = 5.5 Hz, 1H). ^{13}C-NMR (100 MHz, D_2O): δ = 135.25 (s); 131.33 (d); 129.84 (d); 129.45 (d); 126.47 (s); 122.81 (s); 55.45 (d); 40.18 (t); 18.17 (t). MS (EI): m/z = 199 (M^+, 5%); 170 (100%); 122 (89%); 91 (3%). HRMS; Calc. for $C_{12}H_{13}N_3$: M^+ = 199.1107; found: 199.1109.

Example 5:

4-Benzyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (3): According to *GPI* with histamine dihydrochloride (20.0 g, 0.109 mol), NaOH (19.6 g, 0.49 mol), water (100 mL), MeOH (450 mL) and phenacetaldehyde (36 mL, 0.276 mol). The reaction mixture was acidified to pH<1 with aq. conc. HCl (50 mL) and the solvent was removed under reduced pressure. The residue was dried thoroughly under high vacuum and the resulting oil triturated with MeOH (1x150 mL and 2x50 mL). The filtrate was evaporated under reduced pressure and the residue dried under high

vacuum. The resulting oil was triturated with ^{i}PrOH and filtered. The precipitate was dried under high vacuum. **4-Benzyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** was obtained as a colorless powder that still contained 1 eq. ^{i}PrOH (31.9 g, 25 g of product, 96%). ^{1}H-NMR (400 MHz, D_2O): δ = 8.76 (s, 1H); 7.52-7.43 (m, 3H); 7.40-7.35 (m, 2H); 5.07 (dd, J_1 = 9.1 Hz, J_2 = 5.7 Hz, 1H); 3.76 (dt, J_1 = 13.1 Hz, J_2 = 5.2 Hz, 1H); 3.63 (dd, J_1 = 14.4 Hz, J_2 = 5.6 Hz, 1H); 3.53 (ddd, J_1 = 13.9 Hz, J_2 = 7.6 Hz, J_3 = 6.1 Hz, 1H); 3.24 (dd, J_1 = 14.2 Hz, J_2 = 9.3 Hz, 1H); 3.16 (dd, J_1 = 12.9 Hz, J_2 = 7.8 Hz, 1H).

Example 6:

Methyl 4-methyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from **4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (500 mg, 2.38 mmol), K_2CO_3 (690 mg, 5.00 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and methyl chloroformate (0.39 mL, 5.0 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump (MeOH/$CHCl_3$ 0:100 → 0:100 for 5 min, then → 1:3 over 25 min). **Methyl 4-methyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (270 mg, 58%). R_f = 0.30 (MeOH/$CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.52 (s, 1H); 4.99 (s, br., 1H); 4.30 (s, br., 1H); 3.71 (s, 3H); 3.15 (td, br., J_1 = 11.7 Hz, J_2 = 3.7 Hz, 1H); 2.67 (m, 1H); 2.54 (dd, J_1 = 15.6 Hz, J_2 = 4.2 Hz, 1H); 1.88 (d, J = 6.8 Hz, 3H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 157.47 (s); 135.38 (d); 134.32 (s); 126.41 (s); 53.37 (q); 49.43 (d); 38.71 (t); 23.50 (t); 19.28 (q). MS (EI): m/z = 195 (M^+, 11%); 180 (100%); 136 (10%); 120 (16%); 107 (22%). HRMS: Calc. for $C_9H_{13}N_3O_2$: M^+ = 195.1008; found: 195.1010.

Example 7:

Benzyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: According to *GPII*, starting from 4-ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (1.00 g, 4.48 mmol), K_2CO_3 (1.24 g, 9.0 mmol), $CHCl_3$ (10 mL), H_2O (8 mL) and benzyl chloroformate (1.36 mL, 9.0 mmol). After

basic treatment for 1 h the mixture was acidified to pH 8-8.5 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure. Twice successively, the residue was treated with aq. 1M HCl and the solvent removed under reduced pressure. The residue was then suspended in aq. 1M HCl (15 mL) and washed with Et_2O (2x). The aq. phase was evaporated under reduced pressure and the residue purified by RP-HPLC (95% H_2O → 0% H_2O over 20 min. **Benzyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (590 mg, 33%). ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.75 (s, 1H); 7.42-7.27 (m, 5H); 5.19 (s, br., 3H); 4.46 (m, br., 1H); 3.25 (m, br., 1H); 2.78 (m, br., 1H); 2.69 (dd, J_1 = 15.4 Hz, J_2 = 3.4 Hz, 1H); 1.00 (s, br., 3H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 134.09 (d); 129.46 (d); 129.19 (d); 68.90 (t); 52.60 (d); 38.25 (t); 28.04 (t); 10.86 (q). MS (EI): m/z = 285 (M^+, 0.4%); 256 (45%); 194 (34%); 150 (5%); 120 (9%); 107 (5%); 91 (100%). HRMS: Calc. for $C_{16}H_{19}N_3O_2$: M^+ = 285.1477; found: 285.1471. Elemental analysis: Calc. for $C_{16}H_{19}N_3O_2 \cdot C_2HF_3O_2 \cdot H_2O$: C 51.8%, H 5.3%, N 10.6%; found: C 52.0%, H 4.9%, N 9.8%.

Example 8:

Benzyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: According to *GPII*, starting from **4-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (800 mg, 2.54 mmol), K_2CO_3 (737 mg, 5.33 mmol), $CHCl_3$ (6 mL), H_2O (5 mL) and benzyl chloroformate (0.80 mL, 5.33 mmol). After basic treatment for 1 h the mixture was acidified to pH 8 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by RP-HPLC (95% H_2O → 0% H_2O over 20 min). **Benzyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (291 mg, 25%) that contained 0.65 eq. H_2O according to the elemental analysis. t_R = 11.26 min. ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.83 (s, 1H); 7.48-7.27 (m, 10H); 6.48 (s, br., 1H); 5.26 (d, br., J = 10.8 Hz, 1H); 5.18 (d, J = 12.0 Hz, 1H); 4.38 (d, br., J = 12.2 Hz, 1H); 3.20 (ddd, J_1 = 15.9 Hz, J_2 = 11.2 Hz, J_3 = 4.6 Hz, 1H); 2.96-2.78 (m, 2H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 139.04 (s); 137.49 (s); 134.91 (d); 129.89-128.98 (several peaks, d and s); 127.85 (s); 69.11 (t); 54.16 (d); 38.12 (t); 22.24 (t). MS (EI): m/z = 333 (M^+, 9%); 242 (89%); 212 (4%); 198

(61%); 169 (27%); 91 (100%). Elemental analysis: Calc. for $C_{20}H_{19}N_3O_2 \cdot C_2HF_3O_2 \cdot 2/3H_2O$: C 57.5%, H 4.7%, N 9.1%; found: C 57.5%, H 4.4%, N 9.1%.

Example 9:

Benzyl 4-benzyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from **4-benzyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (500 mg, 1.74 mmol), K_2CO_3 (507 mg, 3.67 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and benzyl chloroformate (0.55 mL, 3.67 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump ($MeOH/CHCl_3$ 0:100 → 0:100 for 5 min, then → 1:3 over 25 min). **Benzyl 4-benzyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (225 mg, 42%). $R_f = 0.31$ ($MeOH/CHCl_3$ 1:9). ^{1}H-NMR (400MHz, CD_3OD): δ = 7.57 (s, 1H); 7.23, 7.15 and 7.03 (m, 10H, rot.); 5.33, 5.25, 5.08 and 4.95 (m, 2H, rot.); 4.84 and 4.60 (d, J = 12.2 Hz, 1H, rot.); 4.81 and 4.17 (dd, J_1 = 13.2 Hz and 13.7 Hz, J_2 = 5.4 Hz and 4.6 Hz, 1H, rot.); 3.24-2.90 (m, 3H, rot.); 2.83-2.33 (m, 2H, rot.). ^{13}C-NMR (100 MHz, CD_3OD): δ = 157.24 and 156.95 (s, rot.); 139.24 and 138.79 (s, rot.); 137.46 (s); 135.51 and 135.46 (d, rot.); 130.44 (d); 129.39, 129.24, 129.13, 129.01, 128.93, 128.83 and 128.72 (3xd, rot.); 127.36 (d); 68.31 and 68.17 (t, rot.); 55.24 and 54.53 (d, rot.); 40.96 and 40.20 (t, rot.); 39.73 and 38.97 (t, rot.); 23.39 and 22.88 (t, rot.). MS (EI): m/z = 256 (M^+-C_7H_7, 26%); 212 (22%); 91 (100%). HRMS: Calc. for $C_{21}H_{21}N_3O_2$: M^+ = 347.1634; found: 347.1603.

Example 10:

Benzyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: According to *GPII*, starting from 4-propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (600 mg, 2.52 mmol), K_2CO_3 (720 mg, 5.2 mmol), $CHCl_3$ (6 mL), H_2O (5 mL) and benzyl chloroformate (0.78 mL, 5.2 mmol). After basic treatment for 1h the mixture was acidified to pH 8.5 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (3x) and the combined org. phases

were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by RP-HPLC (85% H_2O → 0% H_2O over 20 min). **Benzyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam that was crystallised from Et_2O (276 mg, 27%). Mp = 166-7 °C. t_R = 8.46 min. ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.74 (s); 7.42-7.27 (m, 5H); 5.31 (m, br., 1H); 5.18 (s, br., 2H); 4.44 (m, br., 1H); 3.25 (m, br., 1H); 2.78 (m, br., 1H); 2.68 (dd, J_1 = 15.6 Hz, J_2 = 3.4 Hz, 1H); 1.76 (m, 2H); 1.44 (m, br., 2H); 0.98 (m, br., 3H). ^{13}C-NMR (100 MHz, CD_3OD); δ = 156.92 (s); 134.08 (d); 130-128 (several peaks, s and d); 68.93 (t); 51.13 (d); 38.15 (t); 36.74 (t); 22.16 (t); 20.27 (t); 14.07 (q). MS (EI): m/z = 300 ($M+H^+$, 20%); 256 (51%); 212 (60%); 208 (28%); 192 (3%); 164 (16%); 120 (12%); 91 (100%). Elemental analysis: Calc. for $C_{17}H_{21}N_3O_2 \cdot C_2HF_3O_2$: C 55.2%, H 5.4%, N 10.2%; found C 55.1%, H 5.1%, N 10.0%.

Example 11:

Methyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: According to *GPII*, starting from **4-ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (600 mg, 2.68 mmol), K_2CO_3 (778 mg, 5.63 mmol), $CHCl_3$ (6 mL), H_2O (4 mL) and methyl chloroformate (0.436 mL, 5.63 mmol). After basic treatment for 1 h the mixture was acidified to pH 8 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by RP-HPLC (95% H_2O over 5 min then → 40% H_2O over 10 min). **Methyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (71 mg, 8%). ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.78 (s, 1H); 4.19 (s, br., 1H); 4.43 (s, br., 1H); 3.75 (s, 3H); 3.22 (m, br., 1H); 2.79 (m, 1H); 2.69 (m, 1H); 1.86 (m, 2H); 1.03 (t, J = 7.6 Hz, 3H). ^{13}C-NMR (100 MHz, d_6-DMSO, at 70 °C): δ = 157.77 (s); 134.06 (d); 129.55 (s); 127.63 (s); 53.74 (q); 52.52 (d); 38.09 (t); 27.92 (t); 22.00 (t); 10.81 (q). MS (EI): m/z = 209 (M^+, 4%); 180 (100%); 150 (4%); 120 (54%); 107 (11%); 94 (15%); 93 (20%); 59 (76%). HRMS: Calc. for $C_{10}H_{15}N_3O_2$: M^+ = 209.1164; found: 209.1171.

Example 12:

Methyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: According to *GPII*, starting from **4-propyl-4,5,6,7-**

tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (600 mg, 2.52 mmol), K_2CO_3 (720 mg, 5.2 mmol), $CHCl_3$ (6 mL), H_2O (4 mL) and methyl chloroformate (0.40 mL, 5.2 mmol). After basic treatment for 1 h the mixture was acidified to pH 8-9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by RP-HPLC (95% H_2O → 40% H_2O over 15 min). **Methyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (134 mg, 16%). ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.78 (s); 5.29 (s, br., 1H); 4.39 (s, br., 1H); 3.73 (s, 3H); 3.25 (s, br., 1H); 2.80 (m, 1H); 2.70 (dd, J_1 = 15.9 Hz, J_2 = 3.9 Hz, 1H); 1.79 (m, 1H); 1.46 (m, 1H); 1.00 (t, J = 7.3Hz, 3H). ^{13}C-NMR (100 MHz, d_6-DMSO, at 70 °C); δ = 155.23 (s); 132.46 (d); 127.74 (s); 125.32 (s); 52.35 (q); 49.05 (d); 36.45 (t); 34.90 (t); 20.49 (t); 18.23 (t); 13.12 (q). MS (EI): m/z = 223 (M^+, 2%); 194 (0.5%); 192 (1%); 180 (100%); 164 (1%); 148 (1%); 121 (6%); 120 (13%); 107 (4%). HRMS: Calc. for $C_{11}H_{17}N_3O_2$: M^+ = 223.1321; found: 223.1323.

Example 13:

Methyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: According to *GPII*, starting from **4-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (800 mg, 2.54 mmol), K_2CO_3 (737 mg, 5.33 mmol), $CHCl_3$ (8 mL), H_2O (5 mL) and methyl chloroformate (0.412 mL, 5.33 mmol). After basic treatment for 1 h the mixture was acidified to pH 8 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by RP-HPLC (95% H_2O → 40% H_2O over 15 min). **Methyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (506 mg, 54%) that contained 1 eq water according to the elemental analysis. ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.84 (s); 7.47-7.24 (m, 5H); 6.46 (s, br., 1H); 4.34 (d, br., J = 11.2 Hz, 1H); 3.79 (s, 3H); 3.18 (ddd, J_1 = 15.9 Hz, J_2 = 11.2 Hz, J_3 = 4.6 Hz, 1H); 2.96-2.86 (m, 1H); 2.82 (dd, J_1 = 15.6 Hz, J_2 = 3.7 Hz, 1H). ^{13}C-NMR (100 MHz, d_6-DMSO, at 70 °C): δ = 154.83 (s); 138.18 (s); 133.75 (d); 128.33 (d); 127.99 (d); 127.26 (d); 127.15 (s); 125.44 (s); 52.56 (q); 52.26 (d); 36.58 (t); 20.64 (t). MS (EI): m/z = 257 (M^+, 100%); 242 (27%); 226 (7%); 198 (22%); 180 (67%); 121 (6%); 120 (11%). HRMS: Calc. for $C_{14}H_{15}N_3O_2$: M^+ =

257.1164; found: 257.1164. Elemental analysis: Calc. for $C_{14}H_{15}N_3O_2 \cdot C_2HF_3O_2 \cdot H_2O$: C 49.4%, H 4.7%, N 10.8%; found: C 49.8%, H 4.8%, N 10.4%.

Example 14:

4-Ethyl-5-(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine trifluoroacetate: According to *GPII*, starting from **4-ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (600 mg, 2.68 mmol), K_2CO_3 (778 mg, 5.63 mmol), $CHCl_3$ (6 mL), H_2O (4 mL) and phenoxyacetyl chloride (0.78 mL, 5.6 mmol). After basic treatment for 1 h the mixture was acidified to pH 9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (3x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by RP-HPLC (85% H_2O → 0% H_2O over 20 min). **4-Ethyl-5-(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine trifluoroacetate** was obtained as foam (490 mg, 46%) that contained 1.5 eq. H_2O according to the elemental analysis. t_R = 5.95 min. ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.72 (s, 1H); 7.25 (t, J = 7.3Hz, 2H); 7.08-6.82 (m, 3H); 5.61 (dd, J_1 = 9.3 Hz, J_2 = 4.6 Hz, 0.9H, 1st rot.); 4.90-4.70 (m, 2 and 0.2H, 2nd rot.); 4.25 (dd, J_1 = 14.4 Hz, J_2 = 5.2 Hz, 0.9H, 1st rot.); 3.52 (ddd, J_1 = 14.9 Hz, J_2 = 12.0 Hz, J_3 = 4.4 Hz, 0.9H, 1st rot.); 3.17 (m, 0.1H, 2nd rot.); 2.93 (m, 1H); 2.76 (m, 1H); 1.10 and 0.97 (t, J = 7.3 Hz, 3H, 2 rot.). ^{13}C-NMR (100 MHz, CD_3OD): δ = 170.08 (s); 159.18 (s); 134.29 (d); 130.48 (d); 129.34 (s); 127.20 (s); 122.60 (d); 115.62 (d); 68.03 (t); 50.38 (d); 39.47 (t); 27.75 (t); 22.86 (t); 10.80 (q). MS (EI): m/z = 285 (M^+, 15%); 256 (60%); 192 (43%); 178 (4%); 150 (13%); 135 (20%); 107 (45%); 77 (100%). HRMS: Calc. for $C_{16}H_{19}N_3O_2$: M^+ = 285.1477; found: 285.1472. Elemental analysis: Calc. for $C_{16}H_{19}N_3O_2 \cdot C_2HF_3O_2 \cdot 3/2H_2O$: C 50.7%, H 5.4%, N 9.8%; found: C 50.6%, H 5.6%, N 9.4%.

Example 15:

4-Propyl-5-(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine trifluoroacetate: According to *GPII*, starting from 4-propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (600 mg, 2.52 mmol), K_2CO_3 (720 mg, 5.2 mmol), $CHCl_3$ (6 mL), H_2O (4 mL) and phenoxyacetyl chloride (0.72 mL, 5.2 mmol). After basic treatment for 1 h the mixture was acidified to pH 8-9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by RP-HPLC (80% H_2O → 0% H_2O over 20 min. **4-Propyl-5-**

(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine trifluoroacetate was obtained as foam (307 mg, 30%) that contained 1.5 eq. H_2O according to elemental analysis. t_R = 6.36 min. ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.74 (s, 1H); 7.30-7.10 (m, 2H); 6.99-6.85 (m, 3H); 5.70 (t, J = 7.1 Hz, 0.9H, 1st rot.); 4.97-4.71 (m, 2H and 0.2H, 2nd rot.); 4.27 (dd, J_1 = 14.6 Hz, J_2 = 5.4 Hz, 0.9H, 1st rot.); 3.54 (ddd, J_1 = 15.3 Hz, J_2 = 11.7 Hz, J_3 = 4.2 Hz, 0.9H, 1st rot.); 3.19 (m, 0.1H, 2nd rot.); 2.94 (ddd, J_1 = 16.9 Hz, J_2 = 11.7 Hz, J_3 = 5.4 Hz, 0.9H, 1st rot.); 2.78 (dd, J_1 = 16.1 Hz, J_2 = 3.7 Hz, 0.9H, 1st rot.); 2.70 (m, 0.2H, 2nd rot.); 1.88 (m, 0.1H, 2nd rot.); 1.80 (m, 0.9H, 1st rot.); 1.52 (m, 0.1H, 2nd rot.); 1.39 (m, 0.9H, 1st rot.); 1.00 and 0.95 (t, J = 7.5 Hz, 3H). ^{13}C-NMR (100MHz, CD_3OD); δ = 170.04 (s); 134.29 (d); 130.49 (d); 129.57 (s); 127.16 (s); 122.63 (d); 115.65 (d); 68.08 (t); 48.86 (d); 39.39 (t); 36.71 (t); 22.89 (t); 20.19 (t); 14.18 (q). MS (EI): m/z = 299 (M^+, 21%); 256 (100%); 206 (64%); 192 (4%); 135 (23%); 120 (40%); 107 (39%); 93 (15%). HRMS: Calc. for $C_{17}H_{21}N_3O_2$: M^+ = 299.1634; found: 299.1630. Elemental analysis: Calc. for $C_{17}H_{21}N_3O_2 \cdot C_2HF_3O_2 \cdot 3/2H_2O$: C 51.8%, H 5.7%, N 9.5%; found: C 51.9%, H 5.6%, N 9.2%.

Example 16:

4-Phenyl-5-(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine trifluoroacetate: According to *GPII*, starting from **4-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (800 mg, 2.54 mmol), K_2CO_3 (737 mg, 5.33 mmol), $CHCl_3$ (8 mL), H_2O (6 mL) and phenoxyacetyl chloride (0.74 mL, 5.33 mmol). After basic treatment for 1 h the mixture was acidified to pH 8-9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by RP-HPLC (85% H_2O → 0% H_2O over 20 min). **4-Phenyl-5-(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine trifluoroacetate** was obtained as foam (400 mg, 35%). t_R = 6.93 min. ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.85 (s, 1H); 7.46-7.23 (m, 7H); 7.00-6.86 (m, 3H); 4.96-4.76 (m, 3H); 4.20 (dd, J_1 = 14.4 Hz, J_2 = 4.9 Hz, 1H); 3.45 (m, 1H); 3.06 (m, 1H); 2.91 (d, J = 15.6Hz, 1H). ^{13}C-NMR (100 MHz, d_6-DMSO): δ = 166.72 (s); 157.72 (s); 138.00 (s); 134.10 (d); 129.27 (d); 128.62 (d); 128.32 (d); 127.77 (d); 127.42 (s); 124.84 (s); 120.89 (d); 114.52 (d); 65.93 (t); 49.70 (d); 37.73 (t); 21.59 (t). MS (EI): m/z = 333 (M^+, 77%); 256 (4%); 240 (100%); 226 (13%); 198 (56%); 169 (48%); 135 (3%); 122 (8%); 120 (12%); 94 (19%); 77 (73%). HRMS: Calc. for $C_{20}H_{19}N_3O_2$: M^+ = 333.1477; found: 333.1475.

Example 17:

Cyclopentyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: According to *GPII*, starting from **4-ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (400 mg, 1.78 mmol), K_2CO_3 (517 mg, 3.74 mmol), $CHCl_3$ (4 mL), H_2O (2 mL) and cyclopentyl chloroformate (511 mg, 3.74 mmol). After basic treatment for 1 h the mixture was acidified to pH 9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (3x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by RP-HPLC (95% H_2O → 65% H_2O over 10 min → 0% H_2O over 10 min). **Cyclopentyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (174 mg, 26%). t_R = 10.14 min. ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.75 (s); 5.17 (s, br., 1H); 5.12 (t, J = 5.4 Hz, 1H); 3.21 (s, br., 1H); 2.76 (m, 1H); 2.68 (dd, J_1 = 14.9 Hz, J_2 = 3.4 Hz, 1H); 1.95-1.58 (m, 10H); 1.02 (t, J = 7.3 Hz, 3H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 157.00 (s); 134.08 (d); 129.71 (s); 127.70 (s); 80.44 (d); 52.48 (d); 37.72 (t); 33.78 (t); 27.86 (t); 24.61 (t); 22.00 (t); 10.95 (q). MS (EI): m/z = 263 (M^+, 4%); 234 (48%); 194 (12%); 178 (12%); 166 (100%); 122 (33%); 120 (14%); 107 (5%), 93 (5%). HRMS: Calc. for $C_{14}H_{21}N_3O_2$: M^+ = 263.1634; found: 263.1595.

Example 18:

Cyclopentyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: According to *GPII*, starting from **4-propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (400 mg, 1.68 mmol), K_2CO_3 (487 mg, 3.53 mmol), $CHCl_3$ (4 mL), H_2O (2 mL) and cyclopentyl chloroformate (482 mg, 3.53 mmol). After basic treatment for 1 h the mixture was acidified to pH 8-9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by RP- HPLC (95% H_2O → 65% H_2O over 10 min → 0% H_2O over 10 min). **Cyclopentyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (106 mg, 27%). t_R = 10.97 min. ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.75 (s, 1H); 5.25 (m, br., 1H); 5.11 (s, br., 1H); 4.38 (m, br., 1H); 3.22 (m, br., 1H); 2.77 (m, br., 1H); 2.68 (dd, J_1 = 15.9 Hz, J_2 = 4.4 Hz, 1H); 1.95-1.58 (m, 10H); 1.46 (m, 12H); 1.00 (t, J = 7.3 Hz,

3H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 134.05 (d); 129.87 (s); 127.67 (s); 80.47 (d); 51.03 (d); 38.10 (t); 36.99 (t); 33.79 (t); 24.59 (t); 21.91 (t); 20.34 (t); 14.12 (q). MS (EI): m/z = 277 (M^+, 1%); 234 (32%); 208 (9%); 192 (10%); 166 (74%); 164 (7%); 150 (4%); 135 (5%); 122 (36%); 120 (49%); 95 (15%); 69 (100%). HRMS: Calc. for $C_{15}H_{23}N_3O_2$: M^+ = 277.1790; found: 277.1780.

Example 19:

Cyclopentyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: According to *GPII*, starting from **4-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (500 mg, 1.59 mmol), K_2CO_3 (461 mg, 3.34 mmol), $CHCl_3$ (5 mL), H_2O (2.5 mL) and cyclopentyl chloroformate (456 mg, 3.34 mmol). After basic treatment for 1 h the mixture was acidified to pH 8-9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by RP-HPLC (95% H_2O → 65% H_2O over 10 min → 0% H_2O over 10 min). **Cyclopentyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (162 mg, 24%) that contained 1eq. H_2O according to the elemental analysis. t_R = 10.35 min. ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.83 (s, 1H); 7.43-7.35 (m, 3H); 7.32-7.27 (m, 2H); 6.44 (s, br., 1H); 5.16 (s, br., 1H); 4.34 (s, br., 1H); 3.18 (m, 1H); 2.91 (dd, J_1 = 16.1Hz, J_2 = 5.9Hz, 1H); 2.83 (dd, J_1 = 16.4 Hz, J_2 = 4.9 Hz, 1H); 1.97-1.56 (m, 8H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 139.24 (s); 134.90 (d); 129.90 (d); 129.84 (d); 129.43 (s); 128.89 (d); 127.38 (s); 80.75 (d); 54.01 (d); 38.01 (t); 33.84 (t); 33.71 (t); 24.58 (t); 22.18 (t). MS (EI): m/z = 311 (M^+, 56%); 242 (100%); 226 (24%); 198 (91%); 169 (72%); 166 (39%); 122 (13%). HRMS: Calc. for $C_{18}H_{21}N_3O_2$: M^+ = 311.1634; found: 311.1625. Elemental analysis: Calc. for $C_{18}H_{21}N_3O_2 \cdot C_2HF_3O_2 \cdot H_2O$: C 54.2%, H 5.5%, N 9.5%; found: C 54.1%, H 5.4%, N 9.4%.

Example 20:

4-Fluorophenyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: According to *GPII*, starting from 4-ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (400 mg, 1.78 mmol), K_2CO_3 (517 mg, 3.74 mmol), $CHCl_3$ (4 mL), H_2O (2 mL) and 4-fluorophenyl chloroformate (0.49 mL, 3.7 mmol). After basic treatment for 1 h the mixture was acidified to pH 9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (3x) and the

combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure, the residue taken in aq. 1M HCl and washed with Et_2O (1x). The aq. phase was evaporated under reduced pressure and the residue was purified by RP-HPLC (90% H_2O → 65% H_2O over 10 min → 5% H_2O over 10 min). **4-Fluorophenyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (64 mg, 9%). t_R = 9.21 min. ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.80 (s, 1H); 7.12 (m, 4H); 5.81 (m, br., 1H); 4.55 (m, br., 1H); 3.44 (m, br., 1H); 2.97 (m, br., 1H); 2.81 (m, br., 1H); 1.96 (m, br., 2H); 1.12 (m, br., 3H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 161.44 (sd, J_F = 182 Hz); 155.77 (s); 148.38 (s); 134.25 (d); 129.36 (s); 127.63 (s); 124.33 (d); 116.76 (sd, J_F = 17 Hz); 53.01 (d); 38.31 (t); 27.62 (t); 22.39 (t); 10.84 (q). MS (EI): m/z = 289 (M^+, 6%); 260 (100%); 178 (77%); 122 (12%); 120 (12%); 112 (7%); 95 (15%). HRMS: Calc. for $C_{15}H_{16}FN_3O_2$: M^+ = 289.1227; found: 289. 1228.

Example 21:

4-Fluorophenyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: According to *GPII*, starting from 4-propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (400 mg, 1.68 mmol), K_2CO_3 (487 mg, 3.53 mmol), $CHCl_3$ (4 mL), H_2O (2 mL) and 4-fluorophenyl chloroformate (0.47 mg, 3.6 mmol). After basic treatment for 1 h the mixture was acidified to pH 8-9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by FC (MeOH/$CHCl_3$ 2:98 → 5:95 → 10:90 → 1:1). **4-Fluorophenyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (92 mg, 18%). R_f = 0.20 (MeOH/$CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.80 (s, br., 1H); 7.03 (m, br., 4H); 7.23 and 4.93 (m, 1H, rot.); 4.45 and 4.36 (m, 1H, rot.); 3.43-3.09 (m, 1H); 2.88-2.76, 2.69-2.46 and 2.32-2.18 (m, 2H, rot.); 1.93-1.33 (m, 2H, rot.); 0.98-0.87 (m, 3H, rot.). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.93 (sd, J_F = 182 Hz); 154.43 (s); 147.15 (s); 134.15 (d); 123.09 (d); 115.88 (dd, J_F = 18 Hz); 53.16 and 52.58 (d, rot.); 38.96 and 38.74 (t, rot.); 37.01 and 36.64 (t, rot.); 23.36 and 22.27 (t, rot.); 19.67 and 19.34 (t, rot.); 14.34 and 14.18 (q, rot.). MS (EI): m/z = 303 (M^+, 2%); 260 (100%); 224 (5%); 208 (7%); 150 (19%); 122 (17%); 112 (10%). HRMS: Calc. for $C_{16}H_{18}FN_3O_2$: M^+ = 303.1383; found: 303.1392.

Example 22:

Methoxy-ethyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from 4-ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (400 mg, 1.78 mmol), K_2CO_3 (517 mg, 3.74 mmol), $CHCl_3$ (4 mL), H_2O (2 mL) and methoxyethyl chloroformate (518 mg, 3.74 mmol). After basic treatment for 1 h the mixture was acidified to pH 9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (3x) and the combined org. phases were dried over Na_2SO_4. The residue was purified by FC ($MeOH/CHCl_3$ 2:98 → 5:95 → 10:90). **Methoxy-ethyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (98 mg, 22%) that contained 0.5 eq. H_2O according to the elemental analysis. R_f = 0.05 ($MeOH/CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.55 (s, 1H); 5.00 (s, br., 1H); 4.35 (m, br., 1H); 4.24 (s, br., 2H); 3.60 (s, br., 2H); 3.35 (s, br., 3H); 3.18 (s, br., 1H); 2.71 (ddd, J_1 = 16.4 Hz, J_2 = 12.0 Hz, J_3 = 5.6 Hz, 1H); 2.53 (dd, J_1 = 15.4 Hz, J_2 = 3.4 Hz, 1H); 1.89 (m, 1H); 1.71 (m, 1H); 1.00 (t, J = 7.3 Hz, 3H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 157.50 (s); 135.22 (d); 133.67 (s); 126.64 (s); 71.86 (t); 65.80 (t); 59.06 (q); 54.81 (d); 39.18 and 38.88 (t, rot.); 28.49 and 28.27 (t, rot.); 23.59 and 23.07 (t, rot.); 11.14 (q). MS (EI): m/z = 253 (M^+, 6%); 224 (100%); 194 (4%); 166 (7%); 150 (3%); 122 (38%). HRMS: Calc. for $C_{12}H_{19}N_3O_3$: M^+ = 253.1426; found: 253.1421. Elemental analysis: Calc. for $C_{12}H_{19}N_3O_3 \cdot 1/2H_2O$: C 54.95%, H 7.68%, N 16.07%; found: C 55.07%, H 7.81%, N 15.78%.

Example 23:

Methoxyethyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from 4-propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (400 mg, 1.68 mmol), K_2CO_3 (487 mg, 3.53 mmol), $CHCl_3$ (4 mL), H_2O (2 mL) and methoxyethyl chloroformate (490 mg, 3.53 mmol). After basic treatment for 1 h the mixture was acidified to pH 8-9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by FC ($MeOH/CHCl_3$ 2:98 → 5:95 → 10:90). **Methoxyethyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (87 mg, 20%) that contained 0.25 eq. H_2O according to the elemental analysis. R_f = 0.25 ($MeOH/CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.51 (s, 1H); 5.08 (s, br., 1H); 4.32 (m, br., 1H); 4.23 (m, br., 2H); 3.59 (s, br., 2H); 3.36 and 3.34 (s, 3H, rot.); 3.17

(m, br., 1H); 2.70 (ddd, J_1 = 16.1 Hz, J_2 = 12.0 Hz, J_3 = 5.6 Hz, 1H); 2.53 (dd, J_1 = 15.4 Hz, J_2 = 3.2 Hz, 1H); 1.79 (m, 1H); 1.70 (m, 1H); 1.45 (m, 2H); 0.97 (t, J = 7.6 Hz, 3H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 157.44 (s); 135.22 (d); 133.93 (s); 126.82 (s); 71.84 (t); 65.79 (t); 59.05 (q); 53.30 (d); 39.10 and 38.80 (t, rot.); 37.71 and 37.46 (t, rot.); 23.59 and 23.06 (t, rot.); 20.49 (t); 14.41 (q). MS (EI): m/z = 267 (M^+, 7%); 224 (100%); 208 (6%); 192 (7%); 180 (12%); 166 (11%); 122 (62%). HRMS: Calc. for $C_{13}H_{21}N_3O_3$: M^+ = 267.1581; found: 267.1582. Elemental analysis: Calc. for $C_{13}H_{21}N_3O_3$ 1/4H_2O: C 57.44%, H 7.97%, N 15.52%; found: C 57.28%, H 8.11%, N 15.22%.

Example 24:

Methoxyethyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from 4-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (500 mg, 1.59 mmol), K_2CO_3 (461 mg, 3.34 mmol), $CHCl_3$ (6 mL), H_2O (4 mL) and methoxyethyl chloroformate (462 mg, 3.34 mmol). After basic treatment for 1 h the mixture was acidified to pH 8-9 with aq. 1M HCl. The reaction mixture was extracted with $CHCl_3$ (4x) and the combined org. phases were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by FC (MeOH/$CHCl_3$ 2:98 → 5:95 → 10:90). **Methoxyethyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (267 mg, 56%). R_f = 0.26 (MeOH/$CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.62 (s, 1H); 7.30 (m, 5H); 6.30 (s, br., 1H); 4.29 (m, br., 2H); 3.65 (m, br., 2H); 3.38 (s, 3H); 3.09 (m, 1H); 2.82 (m, br., 1H); 2.65 (m, br., 1H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 157.09 (s); 141.43 (s); 135.89 (d); 131.30 (s); 129.25 (d); 129.03 (d); 128.77 (d); 128.34 (s); 77.81 (t); 65.99 (t); 59.08 (q); 56.09 (d); 38.95 and 38.81 (t, rot.); 23.51 and 23.07 (t, rot.). MS (EI): m/z = 301 (M^+, 24%); 242 (26%); 198 (41%); 115 (10%); 88 (11%). HRMS: Calc. for $C_{16}H_{19}N_3O_3$: M^+ = 301.1426; found: 301.1419.

Example 25:

Benzyl 4-methyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from **4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (500 mg, 2.38 mmol), K_2CO_3 (690 mg, 5.00 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and benzyl chloroformate (0.75 mL, 5.0 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL)

and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump ($MeOH/CHCl_3$ 0:100 → 0:100 for 5 min, then → 1:3 over 25 min). **Benzyl 4-methyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (193 mg, 30%). R_f = 0.25 ($MeOH/CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.51 (s, 1H); 7.38-7.52 (m, 5H); 5.13 (m, br., 3H); 4.33 (d, br., *J* = 10 Hz, 1H); 3.16 (t, br., *J* = 11.2 Hz, 1H); 2.66 (m, br., 1H); 2.54 (d, br., *J* = 12.9 Hz, 1H); 1.38 (d, *J* = 6.8 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 155.43 and 155.12 (s, rot.); 136.49 (s); 134.00 (d); 132.85 (s); 128.45 (d); 127.98 (d); 127.67 (d); 125.94 and 124.83 (s, rot.); 67.30 (t); 48.36 (d); 37.81 (t); 23.19 and 22.51 (t, rot.); 19.56 and 19.14 (q, rot.). MS (EI): m/z = 271 (M^+, 0.5%); 256 (6%); 180 (82%); 136 (16%); 108 (14%); 91 (100%). HRMS: Calc. for $C_{15}H_{17}N_3O_2$: M^+ = 271.1321; found: 271.1308.

Example 26:

Benzyl 4-benzyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from **4-benzyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (500 mg, 1.74 mmol), K_2CO_3 (507 mg, 3.67 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and benzyl chloroformate (0.55 mL, 3.67 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump ($MeOH/CHCl_3$ 0:100 → 0:100 for 5 min, then → 1:3 over 25 min). **Benzyl 4-benzyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (225 mg, 42%). R_f = 0.31 ($MeOH/CHCl_3$ 1:9). ^{1}H-NMR (400MHz, CD_3OD): δ = 7.57 (s, 1H); 7.23, 7.15 and 7.03 (m, 10H, rot.); 5.33, 5.25, 5.08 and 4.95 (m, 2H, rot.); 4.84 and 4.60 (d, *J* = 12.2 Hz, 1H, rot.); 4.81 and 4.17 (dd, J_1 = 13.2 Hz and 13.7 Hz, J_2 = 5.4 Hz and 4.6 Hz, 1H, rot.); 3.24-2.90 (m, 3H, rot.); 2.83-2.33 (m, 2H, rot.). ^{13}C-NMR (100 MHz, CD_3OD): δ = 157.24 and 156.95 (s, rot.); 139.24 and 138.79 (s, rot.); 137.46 (s); 135.51 and 135.46 (d, rot.); 130.44 (d); 129.39, 129.24, 129.13, 129.01,

128.93, 128.83 and 128.72 (3xd, rot.); 127.36 (d); 68.31 and 68.17 (t, rot.); 55.24 and 54.53 (d, rot.); 40.96 and 40.20 (t, rot.); 39.73 and 38.97 (t, rot.); 23.39 and 22.88 (t, rot.). MS (EI): m/z = 256 (M^+-C_7H_7, 26%); 212 (22%); 91 (100%). HRMS: Calc. for $C_{21}H_{21}N_3O_2$: M^+ = 347.1634; found: 347.1603.

Example 27:

4-Methyl-5-(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine: According to *GPII*, starting from **4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (500 mg, 2.38 mmol), K_2CO_3 (690 mg, 5.00 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and phenoxyacetyl chloride (0.69 mL, 5.0 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump (MeOH/$CHCl_3$ 0:100 → 0:100 for 5 min, then → 1:3 over 25 min). **4-Methyl-5-(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine** was obtained as foam (28 mg, 5%). R_f = 0.12 (MeOH/$CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.55 and 7.53 (s, 1H, rot.); 7.26 (t, J = 7.1 Hz, 2H); 6.99-6.90 (m, 3H); 5.45 and 5.05 (q, J = 6.6 Hz, 1H, rot.); 4.95-4.77 (m, 3H); 4.73 and 4.14 (dd, J_1 = 13.4 Hz and 14.2 Hz, J_2 = 5.4 Hz and 5.1 Hz, 1H, rot.); 3.46 and 3.12 (ddd, J_1 = 12.0 Hz and 12.9 Hz, J_2 = 12.0 Hz and 12.9 Hz, J_3 = 4.2 Hz and 4.9 Hz, 1H, rot.); 2.88-2.54 (m, 2H, rot.); 1.54 and 1.41 (d, J = 6.6 Hz and 6.8 Hz, 3H, rot.). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 166.41 and 166.91 (s); 157.83 (s); 134.29 (d); 129.74 (d); 121.86 (d); 114.74 and 114.63 (d, rot.); 68.18 and 67.47 (t, rot.); 50.15 and 46.78 (d, rot.); 39.81 and 35.94 (t, rot.); 24.03 and 22.04 (t, rot.); 20.52 and 18.91 (q, rot.). MS (EI): m/z = 271 (M^+, 20%); 194 (1%); 178 (100%); 164 (10%); 135 (15%); 107 (44%); 94 (15%).

Example 28:

Allyl 4-methyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from 4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (500 mg, 2.38 mmol), K_2CO_3 (690 mg, 5.00 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and allyl chloroformate (0.53 mL, 5.0 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a

Stem-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump (MeOH/$CHCl_3$ 0:100 → 0:100 for 5 min, then → 1:3 over 25 min). **Allyl 4-methyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (284 mg, 54%). R_f = 0.30 (MeOH/$CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.53 (s, 1H); 6.00-5.85 (m, 1H); 5.29 (ddd, J_1 = 17.2 Hz, J_2 = 3.2 Hz, J_3 = 1.7 Hz, 1H); 5.19 (ddd, J_1 = 10.5 Hz, J_2 = 2.8 Hz, J_3 = 1.3 Hz, 1H); 5.11 (d, br., J = 6.4Hz, 1H); 4.60 (dd, J_1 = 3.9Hz, J_2 = 1.2Hz, 2H); 4.33 (dd, J_1 = 13.4Hz, J_2 = 4.9 Hz, 1H); 3.16 (m, br., 1H); 2.68 (m, 1H); 2.55 (ddd, J_1 = 15.4 Hz, J_2 = 4.2 Hz, J_3 = 1.0 Hz, 1H); 1.39 (d, J = 6.8 Hz, 3H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 156.58 (s); 135.40 (d); 134.31 (s); 134.09 (d); 126.31 (s); 117.73 (t); 67.25 (t); 49.39 (d); 38.71 (t); 23.57 and 23.24 (t, rot.); 19.54 and 19.16 (q, rot.). MS (EI): m/z = 221 (M^+, 2%); 206 (27%); 180 (100%); 136 (30%); 120 (30%); 107 (38%). HRMS: Calc. for $C_{11}H_{15}N_3O_2$: M^+ = 221.1164; found: 221.1160.

Example 29:

Allyl 4-ethyl-3,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from benzyl-4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate (500 mg, 2.23 mmol), K_2CO_3 (646 mg, 4.68 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and allyl chloroformate (0.50 mL, 4.7 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump (MeOH/$CHCl_3$ 0:100 → 0:100 for 5 min, then → 15:85 over 25 min). **Allyl 4-ethyl-3,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (2.2 mg, 0.4%). The low yield is probably due to a leak during the FC. R_f = 0.15 (MeOH/$CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.52 (s, 1H); 5.95 (m, 1H); 5.29 (dd, J_1 = 17.3 Hz, J_2 = 1.2 Hz, 1H); 5.20 (dd, J_1 = 10.5 Hz, J_2 = 1.2 Hz, 1H); 4.99 (m, br., 1H); 4.60 (d, J = 5.1 Hz, 2H); 4.34 (dd, J_1 = 13.4 Hz, J_2 = 4.6 Hz, 1H); 3.19 (m, br.,

1H); 2.70 (dddd, J_1 = 15.6 Hz, J_2 = 12.0 Hz, J_3 = 5.6 Hz, J_4 = 1.2 Hz, 1H); 2.53 (ddd, J_1 = 15.4 Hz, J_2 = 4.2 Hz, J_3 = 1.0 Hz, 1H); 1.88 (dddd, J_1 = 15.1 Hz, J_2 = 15.1 Hz, J_3 = 7.6 Hz, J_4 = 4.6 Hz, 1H); 1.71 (m, 1H); 0.99 (t, J = 7.6 Hz, 3H). MS (EI): m/z = 235 (M^+, 2%); 206 (100%); 194 (16%); 178 (5%); 162 (38%); 150 (4%). HRMS: Calc. for $C_{12}H_{17}N_3O_2$: M^+ = 235.1321; found: 235.1330.

Example 30:

Allyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from 4-propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (500 mg, 2.10 mmol), K_2CO_3 (609 mg, 4.40 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and allyl chloroformate (0.47 mL, 4.4 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump (MeOH/$CHCl_3$ 0:100 → 0:100 for 5 min, then → 1:3 over 25 min). **Allyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (68 mg, 13%). R_f = 0.20 (MeOH/$CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.51 (s, 1H); 5.96 (m, 1H); 5.29 (d, br., J = 17.3 Hz, 1H); 5.19 (dd, J_1 = 10.5 Hz, J_2 = 1.2 Hz, 1H); 5.09 (s, br., 1H); 4.60 (m, 2H); 4.32 (d, br., J = 13.4 Hz, 1H); 3.19 (d, br., J = 11.5 Hz, 1H); 2.70 (m, 1H); 2.55 (dd, J_1 = 15.4 Hz, J_2 = 4.2 Hz, 1H); 1.79 (m, 1H); 1.70 (m, 1H); 1.45 (m, 2H); 0.96 (t, J = 7.3 Hz, 3H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 157.43 (s); 135.38 (d); 134.26(s); 134.14 (d); 126.51 (s); 118.02 and 117.75 (t, rot.); 67.36 (t); 53.46 and 53.30 (d, rot.); 39.10 and 38.81 (t, rot.); 37.71 and 37.45 (t, rot.); 23.62 and 22.97 (t, rot.); 20.51 (t); 14.34 (q). MS (EI): m/z = 249 (M^+, 1%); 206 (44%); 192 (2%); 162 (13%); 135 (4%); 120 (34%); 107 (7%). HRMS: Calc. for $C_{13}H_{19}N_3O_2$: M^+ = 249.1477; found: 249.1468.

Example 31:

2,2,2-Trichloroethyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from 4-ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (500 mg, 2.23 mmol), K_2CO_3 (646 mg, 4.68 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and 2,2,2-trichloroethyl chloroformate (0.64 mL,

4.68 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump ($MeOH/CHCl_3$ 0:100 → 0:100 for 5 min, then → 1:3 over 25 min). **2,2,2-Trichloroethyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (168 mg, 23%). R_f = 0.16 ($MeOH/CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.53 (s, 1H); 5.05 (m, 1H); 4.97-4.72 (m, 2H); 4.39 (m, 1H); 3.25 (m, 1H); 2.76 (m, 1H); 2.58 (dd, J_1 = 15.4 Hz, J_2 = 3.9 Hz, 1H); 1.93 (m, 1H); 1.75 (m, 1H); 1.03 (m, 3H, rot.). ^{13}C-NMR (100 MHz, CD_3OD): δ = 155.57 (s); 135.38 (d); 76.22 and 76.02 (t, rot.); 55.53 (d); 39.47 (t); 28.57 and 28.23 (t, rot.); 23.70 and 22.89 (t, rot.); 11.40 and 11.11 (q, rot.). MS (EI): m/z = 325, 327, 329 (M^+, 2%); 296, 298, 300 (100%); 262 (3%); 178 (19%); 166 (14%); 133 (17%); 122 (38%); 120 (38%); 107 (9%). HRMS: Calc. for $C_{11}H_{14}Cl_3N_3O_2$: M^+ = 325.0152; found: 325.0148.

Example 32:

Allyl 4-benzyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from **4-benzyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (500 mg, 1.74 mmol), K_2CO_3 (507 mg, 3.67 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and allyl chloroformate (0.39 mL, 3.67 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump ($MeOH/CHCl_3$ 0:100 → 0:100 for 5 min, then → 1:3 over 25 min). **Allyl 4-benzyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (63 mg, 12%). R_f = 0.31 ($MeOH/CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.59 (s, 1H); 7.29-6.94 (m, 5H); 5.86 and 5.69 (m, 1H, rot.); 5.32 and 5.23 (m, 1H, rot.); 5.23-5.12 (m, 1H); 5.04 (d, br., J = 12.7 Hz, 1H); 4.49 and 4.29 (m, 2H, rot.); 4.18 and 4.03 (dd, J_1 = 13.4 Hz and 12.7 Hz, J_2 = 4.9 Hz and 4.4 Hz, 1H, rot.); 3.24-2.38 (m, 5H,

rot.). ^{13}C-NMR (100 MHz, CD_3OD): δ = 157.06 and 156.80 (s, rot.); 139.33 and 138.83 (s, rot.); 135.52 (d); 134.08, 133.78 and 133.49 (2x s, rot.); 130.47 (d); 129.21 and 129.12 (d, rot.); 127.54 and 127.32 (d, rot.); 117.67 and 117.55 (t, rot.); 67.17 (t); 55.19 and 54.45 (d, rot.); 40.99 and 40.24 (t, rot.); 39.65 and 38.85 (t, rot.); 23.36 and 22.92 (t, rot.). MS (EI): m/z = 297 (M^+, 0.05%); 240 (3%); 22 (14%); 206 (100%); 162 (21%); 120 (21%); 91 (50%). HRMS: Calc. for $C_{17}H_{19}N_3O_2$: M^+ = 297.1477; found: 297.1448.

Example 33:

2,2,2-Trichloroethyl -4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from 4-propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (500 mg, 2.10 mmol), K_2CO_3 (609 mg, 4.40 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and 2,2,2-trichloroethyl chloroformate (0.61 mL, 4.4 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump (MeOH/$CHCl_3$ 0:100 → 0:100 for 5 min, then → 15:85 over 25 min). **2,2,2-Trichloroethyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam that still contained 0.2 eq. H_2O according to the elemental analysis (196 mg, 27%). R_f = 0.25 (MeOH/$CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.53 (s, 1H); 5.15 (m, br., 1H); 4.85 (m, 2H); 4.36 (m, 1H); 3.26 (m, 1H); 2.76 (m, 1H); 2.58 (d, J = 15.4 Hz, 1H); 2.30 (d, J = 15.1 Hz, 1H); 1.83 (m, 1H); 1.73 (m, 1H); 1.47 (m, 2H); 0.98 (t, J = 7.3 Hz, 1H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 155.53 (s); 135.38 (d); 76.23 and 76.02 (t, rot.); 54.15 and 53.90 (s, rot.); 51.78 and 51.61 (d, rot.); 39.42 and 39.04 (t, rot.); 37.84, 37.37, 37.11 and 36.64 (t, rot.); 23.70, 22.86, 22.27 and 21.56 (t, rot.); 20.74, 20.60, 20.49 and 20.34 (t, rot.); 14.51, 14.45, 14.22 and 14.27 (q, rot.). MS (EI): m/z = 296, 298 and 300 (100%); 262 (4%); 208 (10%); 192 (16%); 166 (24%); 137 (17%); 122 (38%); 95 (25%). HRMS: Calc. for $C_{12}H_{16}Cl_3N_3O_2$: M^+ = 339.0308; found: 339.0318. Elemental analysis: Calc. for $C_{12}H_{16}Cl_3N_3O_2 \cdot 1/5H_2O$: C 41.87%, H 4.80%, N 12.21%; found: C 41.87%, H 4.84%, N 11.81%.

Example 34:

2,2,2-Trichloroethyl -4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from 4-propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (500 mg, 2.10 mmol), K_2CO_3 (609 mg, 4.40 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and 2,2,2-trichloroethyl chloroformate (0.61 mL, 4.4 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump (MeOH/$CHCl_3$ 0:100 → 0:100 for 5 min, then → 15:85 over 25 min). **2,2,2-trichloroethyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam that still contained 0.2 eq. H_2O according to the elemental analysis (196 mg, 27%). R_f = 0.25 (MeOH/$CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.53 (s, 1H); 5.15 (m, br., 1H); 4.85 (m, 2H); 4.36 (m, 1H); 3.26 (m, 1H); 2.76 (m, 1H); 2.58 (d, *J* = 15.4 Hz, 1H); 2.30 (d, *J* = 15.1 Hz, 1H); 1.83 (m, 1H); 1.73 (m, 1H); 1.47 (m, 2H); 0.98 (t, *J* = 7.3 Hz, 1H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 155.53 (s); 135.38 (d); 76.23 and 76.02 (t, rot.); 54.15 and 53.90 (s, rot.); 51.78 and 51.61 (d, rot.); 39.42 and 39.04 (t, rot.); 37.84, 37.37, 37.11 and 36.64 (t, rot.); 23.70, 22.86, 22.27 and 21.56 (t, rot.); 20.74, 20.60, 20.49 and 20.34 (t, rot.); 14.51, 14.45, 14.22 and 14.27 (q, rot.). MS (EI): m/z = 296, 298 and 300 (100%); 262 (4%); 208 (10%); 192 (16%); 166 (24%); 137 (17%); 122 (38%); 95 (25%). HRMS: Calc. for $C_{12}H_{16}Cl_3N_3O_2$: M^+ = 339.0308; found: 339.0318. Elemental analysis: Calc. for $C_{12}H_{16}Cl_3N_3O_2 \cdot 1/5H_2O$: C 41.87%, H 4.80%, N 12.21%; found: C 41.87%, H 4.84%, N 11.81%.

Example 35:

2,2,2-Trichloroethyl 4-benzyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from **4-benzyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride** (500 mg, 1.74 mmol), K_2CO_3 (507 mg, 3.67 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and 2,2,2-trichloroethyl chloroformate (0.51 mL, 3.7 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH

(6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump ($MeOH/CHCl_3$ 0:100 → 0:100 for 5 min, then → 15:85 over 25 min **2,2,2-trichloroethyl 4-benzyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (211 mg, 31%). R_f = 0.22 ($MeOH/CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.61 (s, 1H); 7.27-7.07 (m, 5H); 5.86 and 5.12 (m, 1H, rot.); 4.79-4.63 (m, 1.5H, rot.); 4.83-4.16 (m, 1.5H, rot.); 3.28-3.22 (m, 1H, rot.); 3.20-2.85 (m, 2H, rot.); 2.73-2.63 (m, 1H, rot.); 2.49 and 2.20 (dd, J_1 = 15.4 Hz and 15.6 Hz, J_2 = 3.2 Hz and 3.9 Hz, 1H, rot.). ^{13}C-NMR (100 MHz, CD_3OD): δ = 155.32; 155.13 and 154.98 (s, rot.); 138.94, 138.66, 138.25 and 138.07 (s, rot.); 135.69 and 135.60 (d, rot.); 130.62 and 130.51 (d, rot.); 129.34, 129.21 and 129.06 (d, rot.); 127.69, 127.58 127.45 and 127.39 (d, rot.); 75.97 and 75.88 (t, rot.); 55.41 and 55.13 (s, rot.); 52.84 and 52.70 (d, rot.); 40.89, 40.26 and 40.18 (t, rot.); 39.88, 39.70, 39.50 and 39.29 (t, rot.); 23.42, 22.74, 22.06 and 21.53 (t, rot.). MS (EI): m/z = 387 (M^+, 0.3%); 296, 298 and 300 (100%); 262 (4%); 226 (2%); 166 (22%); 122 (35%). HRMS: Calc. for $C_{16}H_{16}Cl_3N_3O_2$: M^+ = 387.0308; found: 387.0318. Elemental analysis: Calc. for $C_{16}H_{16}Cl_3N_3O_2$: C 49.44%, H 4.15%, N 10.81%; found: C 49.53%, H 4.29%, N 10.36%.

Example 36:

4-Ethyl-5-(4-nitrobenzyl)-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from 4-ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (500 mg, 2.23 mmol), K_2CO_3 (646 mg, 4.68 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and old 4-nitrophenyl chloroformate (1.01 g, 4.68 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump ($MeOH/CHCl_3$ 0:100 → 0:100 for 5 min, then → 1:3 over 25 min). **4-Ethyl-5-(4-nitrobenzyl)-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was

obtained as foam (23 mg, 4%). R_f = 0.11 (MeOH/$CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.17 (d, *J* = 8.8 Hz, 2H); 7.62 (d, *J* = 8.8 Hz, 2H); 7.51 (s, 1H); 3.88 (d, *J* = 14.4 Hz, 1H); 3.74 (d, *J* = 14.4 Hz, 1H); 3.43 (t, *J* = 6.1 Hz, 1H); 3.11 (m, 1H); 2.77 (m, 2H); 2.46 (dt, J_1 = 15.4 Hz, J_2 = 4.5 Hz, 1H); 1.78 (m, 2H); 0.89 (t, *J* = 7.3 Hz, 3H). ^{13}C-NMR (100 MHz, CD_3OD): δ = 149.30 (s); 148.35 (s); 134.81 (d); 130.54 (d); 124.23 (d); 60.23 (d); 57.61 (t); 46.45 (t); 27.43 (t); 20.98 (t); 10.72 (q). MS (EI): m/z = 286 (M^+, 0.4%); 257 (100%); 241 (1%); 227 (1%); 211 (8%); 136 (4%); 122 (7%); 120 (11%). HRMS: Calc. for $C_{15}H_{20}N_4O_2$: M^+ = 286.1430; found: 286.1436.

Example 37:

5-(4-Nitrobenzyl)-4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate: According to *GPII*, starting from 4-propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride (500 mg, 2.10 mmol), K_2CO_3 (609 mg, 4.40 mmol), $CHCl_3$ (6 mL), H_2O (3 mL) and old 4-nitrophenyl chloroformate (949 mg, 4.40 mmol). The reaction was carried out in a parallel fashion in a test-tube closed with a screwed tap and stirred in a *Stem*-stirrer. The basic treatment was carried out in MeOH (6 mL) and aq. 1M NaOH (4 mL). After 1 h the mixture was acidified with aq. 1M HCl (3 mL). The reaction mixture was evaporated in a speed-vac overnight. The residue was triturated with $CHCl_3$ and filtered several times. The combined org. phases were evaporated in a speed-vac. The residue was purified by parallel FC with a gradient pump (MeOH/$CHCl_3$ 0:100 → 0:100 for 5 min, then → 1:3 over 25 min). **5-(4-Nitrobenzyl)-4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate** was obtained as foam (88 mg, 14%). R_f = 0.24 (MeOH/$CHCl_3$ 1:9). ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.14 (d, *J* = 8.8 Hz, 2H); 7.58 (d, *J* = 8.8 Hz, 2H); 7.50 (s, 1H); 3.83 (d, *J* = 14.4 Hz, 1H); 3.74 (d, *J* = 14.4 Hz, 1H); 3.49 (t, *J* = 5.9 Hz, 1H); 3.12 (m, 1H); 2.85-2.70 (m, 2H); 2.44 (ddd, J_1 = 15.9 Hz, J_2 = 5.1 Hz, J_3 = 3.9 Hz, 1H); 1.69 (m, 2H); 1.39 (m, 2H); 0.82 (t, *J* = 7.3 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.03 (s); 147.07 (s); 133.47 (d); 132.38 (s); 129.28 (d); 126.14 (s); 123.53 (d); 57.83 (d); 56.83 (t); 45.02 (t); 36.37 (t); 20.00 (t); 19.40 (t); 14.31 (q). MS (EI): m/z = 299 ($M - H^+$, 0.5%); 257 (100%); 241 (1%); 211 (9%); 136 (4%); 122 (3%); 120 (9%); 106 (3%); 90 (8%). Elemental analysis: Calc. for $C_{16}H_{22}N_4O_2$: C 63.56%, H 7.33%, N 17.06%; found: C 63.00%, H 7.32%, N 17.17%.

Example 38:

Benzyl (*4S,6S*)-4-ethyl-6-[(isobutylamino)-carbonyl]-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: (*4S,6S*)-5-[(Benzyloxy)carbonyl]-4-ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-6-carboxylic acid (99 mg, 0.30 mmol) was dissolved in DMF (2 mL). EDC·HCl (63 mg, 0.33 mmol), HOBt (45 mg, 0.33 mmol), DMAP (cat. amount) and isobutylamine (70 µL, 0.70 mmol) were added. The solution was stirred for 24 h. After removing the solvent under reduced pressure, the residue was purified by RP-HPLC (95% H_2O → 65% H_2O over 10 min → 0% H_2O over 10 min). **Benzyl (*4S,6S*)-4-ethyl-6-[(isobutylamino)-carbonyl]-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (38.8 mg, 34%). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.46 (s, 1H); 7.43-7.31 (m, 5H); 6.50 (s, br., 1H); 5.36 (s, br., 1H); 5.24 (s, br., 3H); 3.35 (d, J = 16.4 Hz, 1H); 3.05 (dt, J_1 = 19.8 Hz, J_2 = 6.7 Hz, 1H); 2.90 (s, br., 1H); 2.82 (dd, J_1 = 16.4 Hz, J_2 = 6.8 Hz, 1H); 1.87-1.74 (m, br., 1H); 1.69 (s, br., 1H); 1.61 (m, 1H); 0.86 (s, br., 9H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 170.82 (s); 157.60 (s); 135.30 (s); 133.16 (d); 128.70 (d); 126.47 (s); 124.79 (s); 69.03 (t); 51.88 (d); 50.73 (d); 47.32 (t); 28.16 (d and t); 20.33 (t); 20.21 (q); 10.97 (q). MS (EI): m/z = 384 (M^+, 11%); 355 (20%); 311 (15%); 284 (6%); 249 (7%); 194 (3%); 150 (8%); 122 (9%); 91 (100%). HRMS: Calc. for $C_{21}H_{28}N_4O_3$: M^+ = 384.2161; found: 384.2172.

Example 39:

Benzyl (*4S,6S*)-6-(aminocarbonyl)-4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate: To a solution of (*4S,6S*)-5-[(Benzyloxy)carbonyl]-4-ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-6-carboxylic acid (80 mg, 0.24 mmol) in DMF (2 mL) were added NH_3/dioxane (0.5M, 1.5 mL, 0.75 mmol), EDC·HCl (48 mg, 0.25 mmol), HOBt (34 mg, 0.25 mmol) and DMAP (cat. amount). The solution was stirred overnight and the solvent removed under reduced pressure. The residue was dried under high vacuum and purified by RP-HPLC (95% H_2O → 65% H_2O over 10 min → 0% H_2O over 10 min). **Benzyl (*4S,6S*)-6-(aminocarbonyl)-4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate** was obtained as foam (32.6 mg, 40%). ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.76 (s, 1H); 7.47-7.21 (m, 5H); 5.48 (s, br., 1H); 5.33-5.10 (m, br., 3H); 3.24 (dd, J_1 = 16.1 Hz, J_2 = 0.7 Hz, 1H); 2.83 (ddd, J_1 = 16.4 Hz, J_2 = 6.8 Hz, J_3 =

1.7 Hz); 1.90-1.73 (m, 2H); 1.06 (s, br., 3H). MS (EI): m/z = 328 (M^+, 4%); 284 (2%); 210 (6%); 193 (14%); 176 (3%); 107 (6%); 91 (100%). HRMS: Calc. for $C_{17}H_{20}N_4O_3$: M^+ = 328.1535; found: 328.1523.

SSAO activity assays

All assays were performed at room temperature with SSAO purified from human umbilical cord arteries. The enzyme activity was measured with two different methods, based on the detection of either hydrogen peroxide or the aldehyde that is formed from SSAO catalysis of its main substrates, primary amines.

Hydrogen peroxide detection

This method is based on the horseradish peroxidase catalyzed hydrogen peroxide oxidation of 10-acetyl-3,7-dihydroxyphenoxazine (Molecular Probes A-6550), that yields a highly fluorescent product, resorufin. Briefly, 10 mM stock solution of substance in DMSO is serially diluted in 0.05 M sodium-potassium phosphate buffer. These dilutions are mixed with benzylamine (SSAO substrate) and a reagent solution consisting of SSAO enzyme, horse radish peroxidase (HRP) and 10-acetyl-3,7-dihydroxyphenoxazine. The final concentrations in the assay volume are 104 µM benzylamine, 219 µM 10-acetyl-3,7-dihydroxyphenoxazine, 1.1 U/ml HRP and a dilution of the SSAO preparation of 1/600. After two hours of incubation in flat-bottomed polystyrene microtiter plates, the fluorescence is measured at 560 ex / 590 em. The inhibition is measured as % decrease of the signal compared to a control containing dilution of DMSO only (no substance).

Aldehyde detection

SSAO activity is measured as increase of aldehyde formed from SSAO degradation of primary amines. Briefly, in conical glass centrifuge tubes, ^{14}C -labeled benzylamine is mixed with substance dilutions (from 10 mM stock solution in DMSO) in 0.05 M sodium-potassium phosphate buffer (pH 7.8). Enzyme, also diluted in phosphate buffer, is added and incubation is performed at room temperature for 60 minutes. The reaction is stopped with 1 M HCl. The formed (^{14}C -labeled) aldehyde is separated from the likewise ^{14}C –labeled benzylamine through extraction with toluene:ethyl acetate and then transferred to liquid scintillation vials for measurement of radioactivity in a beta counter. The final concentrations in the assay volume are 150 µM benzylamine (0.037 MBq/µmol), and a dilution of the SSAO preparation of 1/150.The

inhibition is measured as % decrease of the signal compared to control containing dilution of DMSO only (no substance).

Biological activity

The compounds shown in Tables 2 and 3 were tested for biological activity, determined as per cent inhibition of SSAO at 12 μM concentration of the test compounds. The compounds were shown to inhibit SSAO to from 10 to 97 %.

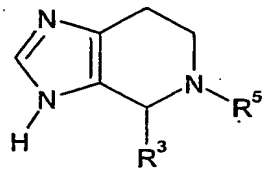


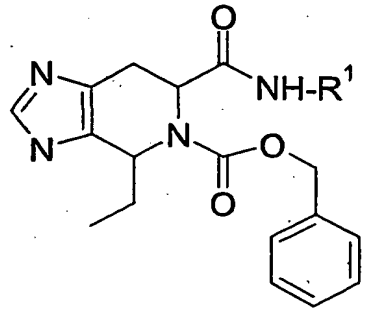
Table 2

Compound	R^3	R^5
4-Methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride	Me	H
4-Ethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride	Et	H
4-Propyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride	Pr	H
4-Phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride	Ph	H
4-Benzyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine dihydrochloride	Bn	H
Methyl 4-methyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Me	Me-OCO-
Methyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Et	Me-OCO-
Methyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Pr	Me-OCO-
Methyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Ph	Me-OCO-
Benzyl 4-methyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Me	Bn-OCO-
Benzyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Et	Bn-OCO-
Benzyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Pr	Bn-OCO-
Benzyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Ph	Bn-OCO-

Compound	R^3	R^5
Benzyl 4-benzyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Bn	Bn-OCO-
4-Methyl-5-(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine	Me	$PhOCH_2CO$-
4-Ethyl-5-(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine trifluoroacetate	Et	$PhOCH_2CO$ -
4-Propyl-5-(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine trifluoroacetate	Pr	$PhOCH_2CO$-
4-Phenyl-5-(phenoxyacetyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine trifluoroacetate	Ph	$PhOCH_2CO$-
Cyclopentyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Et	Cyclopentyl-OCO-
Cyclopentyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Pr	Cyclopentyl-OCO-
Cyclopentyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Ph	Cyclopentyl-OCO-
4-Fluorophenyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Et	4F-Ph-OCO-
4-Fluorophenyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Pr	4F-Ph-OCO-
4-Fluorophenyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	Ph	4F-Ph-OCO-
Methoxyethyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Et	$MeO(CH_2)_2$-OCO-
Methoxyethyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Pr	$MeO(CH_2)_2$-OCO-
Methoxyethyl 4-phenyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Ph	$MeO(CH_2)_2$-OCO-
Allyl 4-methyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Me	CH_2=$CHCH_2$-OCO-
Allyl 4-ethyl-3,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Et	CH_2=$CHCH_2$-OCO-
Allyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Pr	CH_2=$CHCH_2$-OCO-
Allyl 4-benzyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Bn	CH_2=$CHCH_2$-OCO-
2,2,2-Trichloroethyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Et	Cl_3CCH_2-OCO-
2,2,2-Trichloroethyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Pr	Cl_3CCH_2-OCO-
2,2,2-Trichloroethyl 4-benzyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Bn	Cl_3CCH_2-OCO-

Compound	R^3	R^5
4-Ethyl-5-(4-nitrobenzyl)-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Et	4-NO_2-Ph-CH_2-OCO-
5-(4-Nitrobenzyl)-4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate	Pr	4-NO_2-Ph-CH_2-OCO-

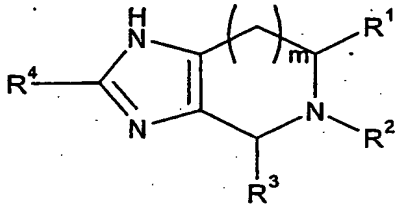
Table 3



Compound	R^1
Benzyl(4S,6S)-4-ethyl-6-[(isobutylamino)-carbonyl]-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate	i-Bu-
Benzyl (4S,6S)-6-(aminocarbonyl)-4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate-trifluoroacetate	H

CLAIMS

1. Use of a compound of Formula (I)



(I)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is

(a) H, or

(b) CONH–R^5;

R^2 is

(a) $COOR^5$,

(b) COR^5,

(c) CONH–R^5,

(d) CSNH–R^5, or

(e) H;

R^3 is

(a) H,

(b) C_{1-8} alkyl, or

(c) $(CH_2)_nAr$;

R^4 is

(a) H,

(b) Ar, or

(c) C_{1-8} alkyl; and

R^5 is

(a) H,

(b) $(CH_2)_nAr$,

(c) $(CH_2)_nOAr$,

(d) C_{1-8} alkyl containing 0-2 oxygen atoms and optionally substituted with 0-5 halogen atoms, or

(e) a polyether chain having the formula $(CH_2)_xO(CH_2)_yO(CH_2)_zCH_3$;

n is an integer 0 to 4;

m is an integer 0 to 2;

x and y are integers 2 to 4;

z is an integer 0 to 3;

Ar is phenyl, 1-naphthyl or 2-naphthyl, unsubstituted optionally mono-or poly-substituted with electrodonating groups, halogen, C_{1-6} alkyl, CF_3, hydroxyl, C_{1-6} alkoxyl, OCF_3, CN, NO_2, phenyloxyl, benzyloxyl, optionally substituted phenyl, alkylsulfonyl, C_{1-6} alkenyl, $-NH_2$, R^7NH-, R^7 R^7N-, C_{1-6} alkylcarboxyl, formyl, C_{1-6} alkyl-CO-NH-, aminocarbonyl (R^7 R^7-N-CO-), SR^7 wherein R^7 is simultaneously or alternatively H or C_{1-6} alkyl; cynnamoyl, unsubstituted or optionally substituted benzyl; 1,1-diphenylethyl, a monocyclic or bicyclic heterocyclic ring (furyl, pyrrolyl, triazolyl, diazolyl, oxazolyl, thiazolyl, oxadiazolyl, isothiazolyl, isoxazolyl, thiadiazolyl, pyridyl, pyrimidyl, pyrazinyl, thienyl, imidazolyl, pyrazolyl, indolyl, quinolinyl, isoquinolinyl, benzofuryl, benzothienyl, benzoxadiazolyl which are unsubstituted or optionally mono or di-substituted with halogen, C_{1-6} alkyl); 2, or 3, or 4-pyridyl or a 5 to 7-membered unsaturated or partially or completely saturated heterocyclic ring each containing 1 to 4 heteroatoms selected from oxygen, nitrogen or sulfur where nitrogen containing heterocycles may contain H or C_{1-6} alkyl or CF_3-CO- at the nitrogen atoms where such a substitution is allowed;

in the manufacture of a medicament for the treatment or prophylaxis of SSAO-mediated complications.

2. The use according to claim 1 wherein R^1 is H.

3. The use according to claim 1 or 2 wherein R^2 is $COOR^5$.

4. The use according to any one of claims 1 to 3 wherein R^3 is C_{1-3} alkyl or benzyl.

5. The use according to claim 1, wherein the compound of Formula (I) is selected from the group consisting of:

benzyl 4-methyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate;

benzyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate;

benzyl 4-propyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate;
2,2,2-Trichloroethyl 4-ethyl-1,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate; and
benzyl (4S,6S)-6-(aminocarbonyl)-4-ethyl-1,4;6,7-tetrahydro-5H-imidazo[4,5-c]pyridine-5-carboxylate trifluoroacetate.

6. The use according to any one of claims 1 to 5, wherein the said SSAO-mediated complication is diabetes.

7. The use according to any one of claims 1 to 5, wherein the said SSAO-mediated complication is a vascular complication.

8. A pharmaceutical formulation for use in the treatment or prophylaxis of an SSAO-mediated complication, comprising as active ingredient a compound as defined in any one of claims 1 to 5, together with a pharmaceutically acceptable carrier.

9. The pharmaceutical formulation according to claim 8, wherein the said SSAO-mediated complication is diabetes.

10. The pharmaceutical formulation according to claim 8, wherein the said SSAO-mediated complication is a vascular complication.

INTERNATIONAL SEARCH REPORT

Inte[illegible]al application No.
PCT/SE 01/02523

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61K 31/437, A61P 31/10, A61P 9/00
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61K, A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-INTERNAL, CHEM.ABS.DATA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 0063208 A1 (NOVO NORDISK A/S), 26 October 2000 (26.10.00)	1-10
A	US 4141899 A (ARCARI ET AL), 27 February 1979 (27.02.79)	1-7
X		8-10
A	GB 2158440 A (FARMITALIA CARLO ERBA S P A), 13 November 1985 (13.11.85)	1-7
X		8-10

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 February 2002	20 -02- 2002
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666.02 86	Authorized officer EVA JOHANSSON/BS Telephone No. +46 8 782.25 00

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 01/02523

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STN International, file CAPLUS, CAPLUS accession no. 1977:479326, document no. 87:79326, Preusser, H. J. et al: "Antimicrobial activity of alkaloids from amphibian venoms and effects on the ultrastructure of yeast cells"; & Anim., Plant Microb. Toxins, Proc. Int. Symp., 4th (1976) Meeting Date 1974, Volume 1, 273-86 --	8-10
A	WO 9323023 A1 (UNIVERSITY OF SASKATCHEWAN), 25 November 1993 (25.11.93) --	1-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

28/01/02

International application No.
PCT/SE 01/02523

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0063208 A1	26/10/00	AU 3956900 A	02/11/00
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